Alcohol and the developing adolescent brain

Despite cannabis, vaping and opioid use garnering significant media attention recently, alcohol is still, by far, the most commonly used substance worldwide[1]. Alcohol use is related to significant health, economic and social burden, and accounts for 5.3% of all deaths in the world every year. It contributes to over 200 medical conditions and is responsible for 5.1% of the global burden of disease and injury[1]. Excessive alcohol use is a pervasive international public health problem that deserves greater attention.

Historically, alcohol use research focused almost solely on adults. A large portion of research in the US was funded in Veterans hospitals, and therefore findings were predominately applicable to older white males. However, over the past two decades, there has been a greater appreciation that alcohol use disorders affect all people, regardless of age, sex, race or ethnicity.

Alcohol use is typically initiated during adolescence, with worldwide estimates indicating that 27% of youth aged 15 to 19 years drank alcohol in the past month[1]. Earlier use of alcohol can have significant implications for problematic use in the future. For example, youth who began drinking before age 15 are four times more likely to develop an alcohol use disorder than youth who do not start drinking until age 21. The odds of subsequently developing problems with alcohol are reduced by 14% with each increasing year of age at first use[2]. These findings are important for prevention programming and encouraging youth to delay their age of first use, a more realistic goal than abstinence-only approaches that have been consistently ineffective[3].

The manner and pattern in which youth use alcohol can differ greatly from adults. Youth tend to drink less frequently than adults, but when they do drink, they tend to drink in much higher quantities, typically in what is referred to as binge drinking episodes (i.e., having 4+ drinks on an occasion for females, and 5+ for males)[4].

The high rates of teen drinking, and binge drinking in particular, are concerning because adolescence is a period of significant neural, social, emotional and cognitive development. While teens may physically look like adults, their brains do not typically reach adult-level maturation until around age 25[5]. Therefore, any disturbances to brain development during this critical growth period could have long-lasting effects.

In the early 2000s, several studies suggested that there was a relationship between alcohol use and brain development. However, due to the cross-sectional nature of these studies, the direction of the relationship was not clear. In the past decade, prospective longitudinal studies have tried to answer the "chicken or egg" question: were the neural abnormalities seen in adolescent heavy drinkers a pre-existing risk factor for initiation of alcohol use, a consequence of heavy drinking, or both?

As it would be highly unethical to randomize youth into "drinking" and "non-drinking" groups, the original studies examining this question were observational[6]. At baseline, only non-drinking youth were enrolled, allowing for assessment of pre-alcohol use cognitive and neural functioning. Naturally, over time, some youth initiated alcohol use, while others remained non-users through adolescence and into young adulthood.

Findings from these studies suggest that it is both the chicken *and* the egg: there are neural and cognitive features that predict who initiates heavy alcohol use during adolescence, and subsequently heavy alcohol use interferes with normal neural developmental trajectories[7].

Specifically, poorer performance on inhibition and working memory tests, smaller gray and white matter brain volume, and altered brain activation during tasks of inhibition, working memory, and reward processing have been related to greater initiation of alcohol use during adolescence.

Once heavy alcohol use is initiated, there are ensuing aberrations in normal development, including poorer inhibition and decision making, atypical maturation of both gray and white matter, and greater brain activation during cognitive tasks, despite equal performance (suggesting that the brains of youth who are drinking have to "work harder" to keep up)[7].

Of course, alcohol is not the only substance that youth typically initiate during adolescence, or the only issue that arises during this developmental period. Larger, multisite studies are currently underway and will help disentangle the complicated picture of concurrent substance use, and the interactive nature of psychopathology, demographics, health habits, and genetic vulnerabilities. These projects include the US Adolescent Brain Cognitive Development (ABCD) and the National Consortium on Alcohol and NeuroDevelopment in Adolescence (NCANDA), as well as the European IMAGEN Consortium. Findings from these investigations will help identify a clearer picture of how alcohol affects neural development.

While these studies will help us learn more about the way alcohol and other substance use affects the developing brain, it is critical that we, as clinicians, utilize this information to inform prevention and treatment of adolescent substance use disorders. Knowing the risk factors for future problematic use can shape educational prevention efforts, while understanding the mechanisms of substance use will improve youth treatment.

This is important, as more effective treatments are desperately needed. Only 6% of adolescents and 8% of young adults who meet criteria for a substance use disorder receive treatment[4]. The current gold standard for adolescent substance use treatment is psychosocial intervention or "talk therapy" (e.g., cognitive behavioral therapy, motivational interviewing, and family therapy)[8]. However, these treatments are only modestly effective, with one-third to one-half of youth returning to substance use within 12 months following treatment.

Utilizing the past two decades of data from the neuroscience field about the effect of substance use on brain development could allow for focused creation of alternative and more efficacious approaches. Neuroscience-informed medications and cognitive interventions that can counter the effects that alco-

hol has had on the brain may enhance the effectiveness of our current treatment options. New techniques to prevent and treat adolescent substance use disorder are necessary to alleviate the extensive public health burden related to this problem at the international level.

In sum, it is clear that alcohol use interferes with cognitive and neural development during adolescence. Early intervention has the potential to prevent substance use escalation and reduce the chronic psychological and physical health problems associated with substance use disorders in adulthood. Our technology has improved significantly over the past two decades and has allowed us to better understand the impact of alcohol use on the developing brain. Translating this information into better prevention and treatment techniques is key in moving the field forward.

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